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### 1. Review Articles

**Ref. 211**  
Beneficial effects of Pycnogenol® in wrinkles - A review.  
The cosmetic treatment of wrinkles.  
*J Cosmet Dermatol, 3(1)*: 26-34.

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*Monograph in Encyclopedia of Dietary Supplements; Ed. Marcel Dekker, digital publisher, 2005,*  
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Matsumori, A. (2007)  
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2. Cardiovascular System

Ref. 216  Pycnogenol® prevents heart failure damage in mice.
Impact of Pycnogenol® on cardiac extracellular matrix remodeling induced by L-NAME
administration to old mice.
Cardiovasc Toxicol, 7: 10-18

Ref. 229  Pycnogenol® counteracts viral infection and prevents development of virus-induced
heart muscle inflammation.
French maritime pine bark extract inhibits viral replication and prevents development of viral
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Pycnogenol Increases the Probability of the Contraction State in Chick Embryonic
Cardiomyocytes, indicating Inotropic Effects.

Ref. 200  Pycnogenol® reduces oedema side effects in hypertensive subjects taking anti-
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Belcaro, G., Cesarone, M.R., Ricci, A., Cornelli, U., Rohdewald, P., Ledda, A.,
Di Renzo, A., Stuard, S., Cacchio, M., Vinciguerra, G., Gizzi, G., Pellegrini, L.,
Control of Edema in Hypertensive Subjects Treated With Calcium Antagonist (Nifedipine) or
Angiotensin-Converting Enzyme Inhibitors With Pycnogenol®.

Ref. 177  Pycnogenol® and Coenzyme Q10 enhance cardiovascular health synergistically.
Nutraceutical Synergism: Pycnogenol® and Coenzyme Q10 Enhance Cardiovascular Health.

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Gulati, O.P. (2005)
The Nutraceutical Pycnogenol®: its role in cardiovascular health and blood glucose control.
**Cardiovascular System**

**Ref. 114**
Review of the positive effects of Pycnogenol® for cardiovascular health, based on the published clinical studies in the cardiovascular area.
Pycnogenol® and cardiovascular health.

**Ref. 080**
Pycnogenol® reduces blood pressure, as shown in a randomized, double-blind, placebo-controlled study performed in mildly hypertensive patients. Furthermore, Pycnogenol® significantly decreases the level of the vasoconstrictor factor (thromboxane) in blood of these patients.
A randomized, double-blind, placebo-controlled, prospective, 16 week crossover study to determine the role of Pycnogenol® in modifying blood pressure in mildly hypertensive patients

**Ref. 117**
Pycnogenol® improves endothelial function of hypertensive patients and helps to lower the dose of the antihypertensive drug (Nifedipine) when administered simultaneously.
Pycnogenol® French maritime pine bark extract, improves endothelial function of hypertensive patients.

**Ref. 017**
Pycnogenol® inhibits the angiotensin II converting enzyme (ACE) and produces a moderate hypotensive effect in rats.
ACE inhibition and hypotensive effect of procyanidinis containing extract from the bark of _Pinus pinaster_ Sol.

**Ref. 036**
Pycnogenol® inhibits smoking induced platelet aggregation in dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin, it does not produce increase in bleeding time.
Inhibition of smoking-induced platelet aggregation by Aspirin and Pycnogenol®.
### Cardiovascular System

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| 053  | **Pycnogenol** inhibits smoking-induced increased levels of thromboxane B₂, the noxious agent involved in the increased platelet reactivity/aggregation in smokers. These results explain the mechanism of anti-platelet aggregation activity of Pycnogenol® observed in smokers.  
Pine bark extract reduces platelet aggregation.  
| 043  | **Pycnogenol** helps fighting against heart disease by inhibiting adhesion and aggregation of platelets and improving microcirculatory blood flow in humans.  
The effect of Pycnogenol® on the microcirculation, platelet function and ischemic myocardium in patients with coronary artery diseases.  
| 027  | **Pycnogenol** counteracts the constriction of blood vessels due to stress. The vasorelaxant activity of Pycnogenol® is mediated through nitric oxide.  
Endothelium-dependent vascular effects of Pycnogenol®.  
| 042  | **Pycnogenol** helps to maintain a healthy circulation through vasodilatation, anti platelet aggregation, free radical scavenging and capillary sealing effects. The role of endothelial nitric oxide (NO) is also discussed.  
Rohdewald, P. (1999)  
Reducing the risk for stroke and heart infarction with Pycnogenol®.  
| 090  | **Pycnogenol** increases antioxidant capacity and lowers cholesterol in obese volunteers in a double-blind, placebo-controlled study.  
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.  
*Lipids, 37(10): 931-934.* |
| 140  | **Pycnogenol** increases red blood cell membrane fluidity and protects erythrocytes against oxidative stress.  
The effect of Pycnogenol® on the erythrocyte membrane fluidity.  
*Gen Physiol Biophys, 23: 39-51.* |
### Ref. 176

Pycnogenol® inhibits the most important pro-inflammatory enzymes, showing a strikingly rapid bioavailability.


Inhibition of Cox-1 and Cox-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).

*Biomed Pharmacother, 60*: 5-9.

### Ref. 230

Pycnogenol® increases endothelium-dependent vasodilation by 42%, by enhancing synthesis of nitric oxide in young healthy men.


Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.

*Hypertens Res, 30*: 775-780.
### 3. Venous Disorders

### Venous Disorders

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<th>Ref.</th>
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<td>Review article: describes efficacy and safety profile of Pycnogenol® in treating venous disorders in humans. Mechanisms of reducing oedema are also discussed.</td>
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*Pycnogenol® is a registered trademark of Horphag Research Ltd.*
Venous Disorders

**Ref. 009**

Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested. Pycnogenol® provides strength to capillary walls and makes them less permeable and thus contributes to anti-oedema, anti-inflammatory effects.


Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonoiderivate bei spontan hypertonischen Ratten.


**Ref. 011**

The efficacy of Pycnogenol® has been confirmed on the basis of objective and subjective signs and symptoms of static oedema in a double blind study in 40 patients suffering from chronic venous insufficiency. Pycnogenol® is a safe veno- protector.


Le pycnogénol: Thérapeutique médicamenteuse de l’œdème statique.


**Ref. 012**

Pycnogenol® produces a vaso-protective effect at the level of capillaries as shown in clinical studies. Pycnogenol® decreases oedema and haemorrhagic tendencies in conditions characterised by increased capillary permeability.


Le pycnogénol: une substance douée de propriétés angioprotectrices dans le traitement de l’insuffisance veineuse chronique.


**Ref. 067**

Pycnogenol® tested in a placebo-controlled, double-blind phase as well as in open phase clinical trial, has been shown to produce significant relief and disappearance of symptoms of chronic venous insufficiency. Safety is confirmed by lack of side effects or changes in blood biochemistry and haematological parameters.


Pycnogenol® in chronic venous insufficiency.


**Ref. 066**

Pycnogenol® tested in a placebo-controlled, double-blind clinical trial, has been shown to produce significant relief and disappearance of symptoms of chronic venous insufficiency.


Pycnogenol® in chronic venous insufficiency.

*Fitoterapia*, 71: 236-244.
Pycnogenol® demonstrated higher efficacy at a lower dosage compared to horse chestnut seed extract in a clinical trial.
Comparative study of Venostasin® and Pycnogenol® in chronic venous insufficiency.
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Efficacia della troxerutina associata al Pycnogenol® nel trattamento farmacologico dell’insufficienza venosa.

Efficacy of Troxerutine in association with Pycnogenol® in the treatment of venous insufficiency
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Prevention of edema in long flights with Pycnogenol®.

### Ref. 134
Pycnogenol® prevents thrombosis and thrombophlebitis in long-haul flights.
Prevention of Venous Thrombosis and Thrombophlebitis in Long-Haul Flights with Pycnogenol®.

### Ref. 135
Zinopin® (a combination of Pycnogenol® and Standardized Ginger Root Extract) - Rationale of its use as Food Supplement in Traveller’s thrombosis and motion sickness.
Review article: Zinopin® - the Rationale for its use as Food Supplement in Traveller’s thrombosis and motion sickness.

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Pycnogenol® inhibits platelet aggregation in a dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin, it does not produce an increase in bleeding time.
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### Ref. 027
Pycnogenol® counteracts the constriction of blood vessels due to stress. The vaso-relaxant activity of Pycnogenol® is mediated through nitric oxide.
Endothelium-dependent vascular effects of Pycnogenol®.

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### 4. Economy class syndrome
Economy class syndrome

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**Ref. 041**

Review article: describes efficacy and safety profile of Pycnogenol® in treating venous disorders in humans. Mechanisms of reducing oedema are also discussed.


Pycnogenol® in venous disorders: A review.


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Pycnogenol® in chronic venous insufficiency.

## 5. Cholesterol Lowering

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## 6. Eye Health

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7. Diabetic Syndrome

Ref. 209 Pycnogenol® inhibits dietary carbohydrate absorption by inhibition of alpha-glucosidase.
Oligomeric procyanidins of French maritime pine bark extract (Pycnogenol®) effectively inhibit alpha-glucosidase.

Ref. 199 Pycnogenol® reduces diabetic microangiopathy.
Improvement of Diabetic Microangiopathy With Pycnogenol®: A Prospective, Controlled Study.
Angiology, 57(4): 431-436.

Ref. 092 The review contains results of 5 clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® supplementation for patients with diabetic retinopathy.
Pycnogenol® for diabetic retinopathy: A review.

Ref. 109 In a dose-finding study Pycnogenol® lowers glucose levels of type II diabetic patients and improves endothelial function.
French maritime pine bark extract Pycnogenol® dose-dependently lowers glucose in type II diabetic patients.
Diabetes Care, 27(3): 839.

Ref. 195 Pycnogenol® accelerates healing of diabetic ulcers.
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®
### Diabetic Syndrome

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Ref. 090 Pycnogenol® supplementation reduced blood levels of the “bad” cholesterol LDL in human volunteers.

Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.

*Lipids*, 37(10): 931-934.

Ref. 043 Pycnogenol® helps fighting against heart disease by inhibiting adhesion and aggregation of platelets and improving microcirculatory blood flow in humans.

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Ref. 114 Review of the positive effects of Pycnogenol® for cardiovascular health, based on the published clinical studies in the cardiovascular area.

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Ref. 042 Pycnogenol® helps to maintain a healthy circulation through vasodilatation, anti-platelet-aggregation, free radical scavenging and capillary sealing effects. The role of endothelial nitric oxide (NO) is also discussed.

Rohdewald, P. (1999)
Reducing the risk for stroke and heart infarction with Pycnogenol®.

### 8. Anti-Aging

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| 098  | Pycnogenol® delays the aging process as shown by an increased life-span of fruit flies.  
Role of Pycnogenol® in aging by increasing the Drosophila's life-span.  
| 099  | Pycnogenol® in combination with other antioxidants administered as a dietary supplement increases life-span of mice. The findings support its beneficial effects against neurogenerative diseases.  
Reduction of inclusion body pathology in ApoE-deficient mice fed a combination of antioxidants.  
| 052  | Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.  
Pycnogenol® improves learning impairment and memory deficit in senescence-accelerated mice.  
| 029  | Pycnogenol® slows down the aging related process of decline in activities of immune- and blood cells generating systems and restores their functions to normal.  
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.  
| 069  | Pycnogenol® produces significant reduction in vascular damage caused by β-amyloid protein. β-amyloidosis is one of the neuropathological hallmarks of Alzheimer's disease (AD). This explains the role of Pycnogenol® in reducing the risk of AD.  
Pycnogenol® protects vascular endothelial cells from β-amyloid-induced injury.  
Neuronal apoptosis (early cell death) is induced by the amyloid-β-peptide in the brain of Alzheimer patients. In vitro experiments demonstrated an inhibition of cell death of neurons by Pycnogenol®.

Pycnogenol® protects neurones from amyloid β peptide-induced apoptosis. 
9. Inflammation

Ref. 208  
Pycnogenol® in vitro study provides evidence of chemoprevention.  
Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.  

Ref. 202  
Pycnogenol® reduces symptoms of knee osteoarthritis.  
Effect of Pine Bark Extract (Pycnogenol®) On Symptoms Of Knee Osteoarthritis.  

Ref. 185  
Pycnogenol® inhibits key triggers of inflammation.  
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).  

Ref. 176  
Pycnogenol® inhibits the most important pro-inflammatory enzymes, showing a strikingly rapid bioavailability.  
Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).  

Ref. 107  
The tissue destroying enzymes (matrix metalloproteinases) collagenase, elastase and gelatinase are inhibited in vitro. Release of these enzymes from inflammatory cells is also inhibited by Pycnogenol® and its metabolites.  
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).  
Inflammation

Ref. 180   Pycnogenol®’s beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc.
Nutritional supplements in clinical practice.
Progr Med, 24: 1503-1510.

Ref. 010   Pycnogenol® scavenges superoxide radicals in vitro and inhibits oedema in vivo. The anti-inflammatory and free radical scavenging activities are closely correlated.
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of Pinus pinaster sol. and its fractions.

Ref. 183   Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histomorphological evidence in rats.
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.

Ref. 111   Pycnogenol® applied topically after sunburn inhibits photocarcinogenesis.
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.

Ref. 013   Applied topically, Pycnogenol® significantly reduces UVB radiation induced-erythema, the procyanidins are the protecting factors.
Anti-inflammatory activities of procyanidin-containing extracts from Pinus pinaster sol.

Ref. 019   Pycnogenol® produces an anti-oedema effect in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.
Antiinflammatory activities of procyanidin containing extracts from Pinus pinaster Ait. after oral and cutaneous application.
Pharmazie, 52(5): 380-382.
Inflammation

Ref. 193  Oral administration of Pycnogenol® is able to delay and to reduce skin cancer following UV radiation. 
Cancer chemopreventive effects of Pinus maritima bark extract on ultraviolet radiation and ultraviolet radiation -7,12 dimethylbenz(a) anthracene induced skin carcinogenesis of hairless mice. 

Ref. 074  Pycnogenol® inhibits UV-induced erythema in humans. This effect was concentration dependent indicating the beneficial effects of Pycnogenol® in skin disorders induced by UV radiation. 
Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by French maritime pine bark extract. 
10. Skin Care

Ref. 211 Beneficial effects of Pycnogenol® in wrinkles- A review article.
The cosmetic treatment of wrinkles.

Ref. 172 Ulcers of the lower legs heal faster after oral plus topical application of Pycnogenol®.
Venous Ulcers: Microcirculatory Improvement and Faster Healing with Local Use of Pycnogenol®.

Ref. 195 Pycnogenol® accelerates healing of diabetic ulcers.
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®.

Ref. 133 Pycnogenol® dose-dependently speeds-up the wound healing process and reduces scar formation.
Short communication: Pycnogenol® accelerates wound healing and reduces scar formation.
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Ref. 081 Pycnogenol® shows beneficial effects in melasma.
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*Phytother Res*, **16**: 567-571.

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Schönlau, F. (2002)
The cosmeceutical Pycnogenol®.
*J Appl Cosmetol*, **20**: 241-246.
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<td><strong>Pycnogenol® produces an anti-oedema effect in two different models.</strong> Topical application of Pycnogenol® gel protects the skin against UV radiation.&lt;br&gt;Blazso, G., Gabor, M. and Rohdewald, P. (1997)&lt;br&gt;Anti-inflammatory activities of procyanidin containing extracts from Pinus pinaster Ait. after oral and cutaneous application.&lt;br&gt;<em>Pharmazie, 52(5)</em>: 380-382.</td>
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Ref. 008  Pycnogenol® protects the skin from ultraviolet-radiation-induced oxidative stress injury (lipid peroxidation and cytotoxicity). The protective effects were related to dose, with the highest concentration providing the greatest benefits.
Ultraviolet radiation-induced oxidative stress in cultured human skin fibroblasts and antioxidant protection.

Ref. 073  Pycnogenol® affects favourably the gene expression profile in human keratinocytes in vitro, thus having a great potential in treatment of psoriasis and dermatoses.
From ancient remedies to modern therapeutics: Pine bark uses in skin disorders revisited.
*Phytother Res*, 15: 76-78.

Ref. 137  Evidence of percutaneous absorption of Pycnogenol® in human skin.
*In vitro Percutaneous Absorption of Pine Bark Extract (Pycnogenol®) in Human Skin.*

Ref. 107  The tissue destroying enzymes (matrix metalloproteinases) collagenase, elastase and gelatinase are inhibited in vitro. Release of these enzymes from inflammatory cells is also inhibited by Pycnogenol® and its metabolites.
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).

Ref. 185  Pycnogenol® inhibits key triggers of inflammation.
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).

Ref. 057  Pycnogenol® inhibits Interferon-γ (IFN-γ)-induced ICAM-1 expression in human skin cells (keratinocytes). This effect is dose and time dependent indicating the therapeutic potential of Pycnogenol® in inflammatory skin disorders.
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Ref. 150  Pycnogenol® shows antimicrobial activity in vitro.
Anti-microbial activity of Pycnogenol®.

Ref. 030  Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.

Ref. 026  Pycnogenol® protects α-tocopherol in endothelial cells.
Procyanidins extracted from pine bark protect α-tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide peroxynitrite.

Ref. 009  Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested. Pycnogenol® provides strength to capillary walls and makes them less permeable and thus contributes to anti-oedema, anti-inflammatory effects.
Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonederivate bei spontan hypertonischen Ratten.
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A Pycnogenol®-containing chewing gum tested in a clinical trial reduced bleeding of the gum and plaque formation on the teeth.
Pycnogenol® chewing gum minimizes gingival bleeding and plaque formation.
*Phytomedicine*, 9: 410-413.

Ref. 009
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12. Immunology

Ref. 082 Pycnogenol® shows beneficial effects in case of lupus erythematosus.
Pycnogenol® Efficacy in the Treatment of Systemic Lupus Erythematosus Patients.

Ref. 029 Pycnogenol® slows down the aging related process of decline in the activities of immune- and blood cells generating systems and restores their functions to normal.
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.

Ref. 016 Pycnogenol® enhances the activity of the immune system in mice infected with a leukemia-causing retrovirus. Pycnogenol® increases the natural killer cell cytotoxicity.
Immunomodulation by Pycnogenol® in retro-virus infected or ethanol-fed mice.

Ref. 055 Pycnogenol® increases TNF-α secretion in the macrophage system in a concentration and time dependent manner indicating that it acts as modulator of the immune response in macrophages.
Activity of monomeric, dimeric, and trimeric flavonoids on NO production, TNF-alpha secretion, and NF-kappaB-dependent gene expression in RAW 264.7 macrophages.

Ref. 095 Pycnogenol® activates in vitro macrophages to kill more effectively invading bacteria.
Pycnogenol® augments macrophage phagocytosis and cytokine secretion.

Ref. 111 Pycnogenol® applied after sunburn inhibits UV-induced suppression of immune system.
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.
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Matsumori, A. (2007)  
Treatment Options in Myocarditis.  
| 173  | Pycnogenol® selectively kills cancerous ovarian germ cells.  
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| 059  | Pycnogenol® selectively kills cancerous human mammary cells (MCF-7), without affecting the normal mammary cells (MCF-10).  
Selective induction of apoptosis in human mammary cancer cells (MCF-7) by Pycnogenol®.  
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| 208  | Pycnogenol® reduces cancerogenesis in human ovarian cells.  
Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.  
| 221  | Pycnogenol® inhibits the harmful effects of two mutagenic chemicals.  
Antimutagenic In Vitro Activity of Plant Polyphenols: Pycnogenol® and *Ginkgo biloba* Extract (EGb 761).  
13. Allergies and Asthma

Ref. 077 Pycnogenol® reduces asthma symptoms and improves lung function of asthmatic patients in a placebo-controlled, cross-over study.

Ref. 149 Pycnogenol® improves pulmonary functions and reduces symptoms of asthma in children.
*J Asthma*, **41**(8): 825-832.

Ref. 089 Pycnogenol® blocks release of histamine from mast cells in vitro to the same extent as the antiasthmatic drug DNCG.
## 14. Sport & Endurance

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| 230  | Pycnogenol® increases vasodilation by 42% in young health men to warrant, sufficient blood and oxygen supply to performing muscle.  
Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.  
*Hypertens Res, 30*: 775-780. |
| 044  | Pycnogenol® increases human endurance during exercise by 21% providing antioxidant reserves.  
Improved endurance by use of antioxidants.  
| 189  | Pycnogenol® reduces muscular pain and cramps in athletes and in patients with chronic venous insufficiency, diabetes or poor circulation in the legs.  
Cramps and Muscular Pain: Prevention with Pycnogenol® in Normal Subjects, Venous Patients, Athletes, Claudicants and in Diabetic Microangiopathy.  
| 096  | Pycnogenol® stimulates Human Growth Hormone (HGH) secretion in vitro thousand times more effectively than other natural compounds. Treatment with HGH increases muscle mass and decreases fat mass.  
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### 15. Menstrual Disorders, Pregnancy Associated Pain and Endometriosis

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| Effect of French Martime Pine Bark Extract on endometriosis as compared with Leuprolein acetate.  

| Ref. 174 | Pycnogenol® reduces low-back pain in late period of pregnancy.  
| Pycnogenol® Alleviates Pain Associated with Pregnancy.  

| Ref. 145 | Pycnogenol® produces analgesic effect in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.  
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Menstrual Disorders, Pregnancy Associated Pain and Endometriosis

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Antispasmodic activity on rat smooth muscle of polyphenol compounds caffeic and protocatechic acids.

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Effect of Pycnogenol®, French Maritime Pine Bark Extract, on Dysmenorrhea: a multicenter, randomized, double-blind, placebo-controlled study.
*J Reprod Med*, in print

Ref. 187  Pycnogenol® improves a broad range of climacteric symptoms in menopausal women.
A randomized, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.
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16. Fertility

Ref. 046  Pycnogenol® improves the morphology of spermatozoa. The percentage of non-deformed sperms in sub-fertile men was increased by 99% after supplementation with Pycnogenol® for three months.
Improvement of sperm quality by Pycnogenol®.

Ref. 091  After treatment with Pycnogenol® increase in functionally normal sperm may allow infertile couples to forgo in vitro fertilization.
Improvement in sperm quality and function with French maritime pine tree bark extract.

Ref. 143  Pycnogenol® and Ginkgo biloba supplementation showed beneficial effects in erectile dysfunction.
The effect of natural polyphenols (Extract from Pinus pinaster (Pycnogenol®) and Ginkgo biloba (EGB 761) on the oxidative stress and erectile function in patients suffering from erectile dysfunction.
Proceedings. (Abstract No L 61)
### 17. Attention Deficit Hyperactivity Disorder (ADHD)

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Title</th>
<th>Authors</th>
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<tbody>
<tr>
<td>047</td>
<td>Positive experience with Pycnogenol® in treating ADHD is mentioned in this letter to the Editor.</td>
<td>Heimann, S.W. (1999)</td>
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<tr>
<td>048</td>
<td>Pycnogenol® is recommended for treatment of Attention Deficit Disorder.</td>
<td>Hanley, J.L. (1999)</td>
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**Ref. 205**

Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).


Research Article: The effect of polyphenolic extract from pine bark, Pycnogenol®, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).


**Ref. 204**

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*Free Radic Res, 40(9): 1003-1010.*

**Ref. 190**

Pycnogenol® provides relief of hyperactivity and improves attention in children with ADHD in a double-blind placebo controlled study.


Treatment of ADHD with French maritime pine bark extract, Pycnogenol®.


**Ref. 047**

Positive experience with Pycnogenol® in treating ADHD is mentioned in this letter to the Editor.


Pycnogenol for ADHD?


**Ref. 048**

Pycnogenol® is recommended for treatment of Attention Deficit Disorder.

Hanley, J.L. (1999)

Attention Deficit Disorder.

*Impact Communications Inc., Green Bay, WI, USA, 17-19.*
Ref. 231  Pycnogenol® lowers stress-hormones in children with ADHD.
Urinary catecholamines in children with attention deficit hyperactivity disorder (ADHD): modulation by a polyphenolic extract from pine bark (Pycnogenol®).
_Nutr Neurosci_, in print.
# 18. Antioxidant and Free Radical Scavenger

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Title</th>
<th>Authors</th>
<th>Journal details</th>
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Antioxidant and Free Radical Scavenger

Ref. 021 Pycnogenol® is shown to be the strongest hydroxyl and superoxide radical scavenger among other extracts tested. In addition, Pycnogenol® is resistant to heat and ascorbate oxidase.

Ref. 030 Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.

Ref. 026 Pycnogenol® protects α-tocopherol in endothelial cells.

Ref. 033 Pycnogenol® is an efficient antioxidant due to the relative stability of its corresponding radical and its regeneration by vitamin C and vitamin E homologue Trolox.

Ref. 025 Pycnogenol® inhibits the effect of oxidative stress and minimises hydroxyl radical-induced DNA damage in vitro.

Ref. 020 Pycnogenol® stimulates synthesis of antioxidative enzymes inside cells of the arteries thereby doubling the amount of antioxidative enzymes.
Ref. 072  Pycnogenol® selectively enhances activity of intracellular antioxidative enzymes.
Pycnogenol® inhibits generation of inflammatory mediators in macrophages.

Ref. 105  Pycnogenol® lowers blood glucose and increases intracellular antioxidant defense mechanism in diabetic rats.
Effect of Pycnogenol® treatment on oxidative stress in streptozotocin-induced diabetic rats.

Ref. 051  Pycnogenol® protects retina of the eye against damage caused by oxidative stress. The effect is more pronounced when compared to other antioxidant bioflavonoids. Pycnogenol® enhances the effects of other antioxidants like Coenzyme Q10 when combined together.
In vitro testing of antioxidants and biochemical end-points in bovine retinal tissue.

Ref. 010  Pycnogenol® scavenges superoxide radicals in vitro and inhibits oedema in vivo. The anti-inflammatory and free radical scavenging activities are closely correlated.
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of Pinus pinaster sol. and its fractions.

Ref. 014  Pycnogenol® protects the endothelial cells which line the blood vessels from free radicals damage. Damage to endothelial cells is considered a prime cause for atherosclerosis.
Pycnogenol® protects vascular endothelial cells from t-butyl hydroperoxide induced oxidant injury.

Ref. 070  Pycnogenol® by virtue of its high content of procyanidins is more potent antioxidant than other herbal-sourced antioxidants containing relatively higher content of regular flavon(ol)s. This fact is explained on structural and functional basis.
Bors, W., Michel C and Stettemaier, K (2000)
Electron paramagnetic resonance studies of radical species of proanthocyanidins and gallate esters.
Ref. 022  Pycnogenol® in addition to its free radical scavenging property, modulates the production of nitric oxide radicals in activated inflammatory cells.
Procyanidins extracted from Pinus maritima (Pycnogenol®): scavengers of free radical species and modulators of nitrogen monoxide metabolism in activated murine raw 264.7 macrophages.

Ref. 062  Pycnogenol® blocks oxidative modification of cellular proteins more effectively than other antioxidants.
Effect of select antioxidants on malondialdehyde modification of proteins.
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Ref. 063  Pycnogenol® shows free radical scavenging activity against reactive oxygen species.
It inhibits the generation of pro-inflammatory mediators confirming the anti-inflammatory and immuno-modulatory profile of Pycnogenol®.
Effect of bioflavonoids extracted from the bark of Pinus maritime on proinflammatory cytokine interleukin-1 production in lipopolysaccharide-stimulated raw 264.7.

Ref. 007  Pycnogenol® is proven an excellent radical scavenger of enzymatically produced hydroxyl and singlet oxygen free radicals, two of the most dangerous free radicals.
Radical scavenger properties of leucocyanidine.

Ref. 086  Pycnogenol® in combination with whey increases antioxidative capacity of plasma.
Determination of the antioxidative potential of human plasma after supplementation with Pycnogenol® and whey.
Food Res Intern, 35: 257-266.

Ref. 218  Pycnogenol® lowers oxidative stress in the liver of rats challenged with a chemical toxin.
Ameliorative Effects of Pycnogenol® on Carbon Tetrachloride-Induced Hepatic Oxidative Damage in Rats.
Phytother Res, in print.


Ref. 227  Pycnogenol® and Lutein display synergistic antioxidant effects for prevention of lipid peroxidation.
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.

Ref. 215  Pycnogenol® protects liposomes from lipid peroxidation and shows synergistic protective effects with vitamin C and vitamin E.
The Combined Effect of Pycnogenol® with Ascorbic Acid and Trolox on the Oxidation of Lipids and Proteins.
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## 19. Bio-Availability and Metabolism

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Rohdewald, P. (1999)  
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| Ref. 058 | Pycnogenol®, its components and metabolites are bio-available in human for more than 24 hours to produce their beneficial effects.  
Urinary metabolites of French maritime pine bark extract in humans.  
| Ref. 060 | Bio-kinetics (absorption, metabolism and excretion) of Pycnogenol® in healthy human subjects has been demonstrated by studying the excretion pattern of ferulic acid (one of the components of Pycnogenol®).  
Ferulic acid excretion as a marker of consumption of a French maritime pine (*Pinus maritima*) bark extract.  
| Ref. 137 | Evidence of percutaneous absorption of Pycnogenol® in human skin.  
*In vitro* Percutaneous Absorption of Pine Bark Extract (Pycnogenol®) in Human Skin.  
| Ref. 197 | Pycnogenol® is bioavailable after oral administration.  
Single and multiple dose pharmacokinetics of maritime pine bark extract (Pycnogenol®) after oral administration to healthy volunteers.  
20. Anti-microbial and anti-viral activity

Ref. 150  Pycnogenol® shows antimicrobial activity in vitro.
Short Communication: Antimicrobial activity of Pycnogenol®.

Ref. 229  Pycnogenol® inhibits viral replication in the heart muscle of mice.
French maritime pine bark extract inhibits viral replication and prevents development of viral myocarditis.
J Card Fail, 20, in print.

Ref. 225  Pycnogenol® inhibits growth of Helicobacter pylori and their adherence to mucosal cells of the stomach.
In vitro inhibition of Helicobacter pylori growth and adherence to gastric mucosal cells by Pycnogenol®.
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### 21. Joint Health

| Ref. 223 | Pycnogenol® improves pain and mobility and lowers required pain medication in osteoarthritis.  
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Pycnogenol® supplementation reduces pain and stiffness and improves physical function in adults with knee osteoarthritis.  
*Nutr Res*, in print. |

| Ref. 176 | Pycnogenol® consumption non-selectively, inhibits cox enzyme, which are involved in pain sensation during inflammation.  
Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).  
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| Ref. 185 | Pycnogenol® inhibits key trigger of inflammation.  
Inhibition of NF-κB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).  

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Antioxidant activity and inhibition of matrix-metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).  
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